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A HealthTech Report

HealthTech V Annual Report - Year 4

October 1, 2014 to September 30, 2015

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Highlights

- Alternative Methods for Delivery of Antiretroviral Drugs team created physical prototypes of applicator for vaginal delivery of dissolving microneedle patch for use in market research and finalized the focus group discussion guides for potential users and health care providers, concept descriptions, and project plan with Added Value, a market research organization in South Africa.

- Amoxicillin Dispersible Tablet team hosted a meeting in New York City on May 28, 2015, with various stake holders and completed all revisions of the user-friendly product presentation and job aid and disseminated to meeting participants and other stakeholders in August 2015. The team also finalized the protocol and data collection tools in collaboration with the study team in Kenya and submitted for review by a local ethical review board.

- Chlorhexidine for Umbilical Cord Care team participated in the stakeholder meeting in Nigeria in September 2015 to discuss a national scale-up strategy. The team also developed the introduction and monitoring and evaluation plans to introduce the chlorhexidine product in ten counties in Western and Nyanza regions in Kenya and in collaboration with the United States Pharmacopeia (USP) selected appropriate manufacturers for production of the chlorhexidine product in Kenya.

- Cold Chain Equipment Inventories team's data collection forms will be posted by UNICEF on the TechNet website at the end of 2015. This is a step toward formalizing a data standard for cold chain equipment inventories under the logos of UNICEF and Gavi

- Innovation Countdown 2030 team developed a quantitative methodology to assess maternal, neonatal, and child health innovations. Disease area models were generated for eight maternal, child, and neonatal health innovations. The models estimated lives saved, percent reduction in deaths, and intervention and downstream costs between 2015 and 2030. The modeling results were presented in the inaugural IC2030 report *Reimagining Global Health.*

- The IMPT Secretariat completed a comprehensive update to the MPT Product Development Pipeline Database in June 2015 and also finalized the structure for the new, user-friendly MPT resource center on the CAMI Health website.

- Injectable Antibiotics for Newborn Sepsis Treatment team completed the landscape of alternative formulations of gentamicin along with the landscape of alternative delivery platforms. The landscape, named *Gentamicin for Treatment of Neonatal Sepsis: A Landscape of Formulation, Packaging, and Delivery Alternatives*.

- Neonatal Resuscitators team completed version 1 of the Neonatal Resuscitation Commodities Procurement Toolkit and shared with the ministry of health and nongovernmental organization procurement personnel and other program managers in Malawi, Tanzania, and Uganda through

technical assistance workshops in November 2014. Beginning in June 2015 the team also disseminated tools generated through HealthTech (Guide to Selection, Quantification Tool, S&T Purchasing Guides) and other tools (Procurement Toolkit).

- Noninvasive Anemia Screening team established a clinical trial agreement between all parties including Masimo, the developer of the noninvasive hemoglobin screening device. The team also launched recruitment and enrollment in the study at the pediatric clinic at the University Teaching Hospital of Kigali in Rwanda.
- SILCS (Caya) Diaphragm team has received approvals for two CONRAD clinical studies.
- Caya® diaphragm received Australian regulatory approval in late 2014 distribution was launched.
- Caya® diaphragm was registered in Malaysia, and a pilot activity was initiated to gauge feasibility of introduction among family planning providers.
- Caya® product launch happened in the United States in June 2015.

HealthTech Projects

Alternative Methods for the Delivery of HIV Antiretroviral Drugs

Goal

Investigate the feasibility of alternative delivery systems for the use of long-acting antiretroviral drugs for HIV preexposure prophylaxis (PrEP).

Status of the project as of September 30, 2015

In Year 3, HealthTech conducted a landscape analysis and developed a target product profile of potential alternative delivery methods for rilpivirine for HIV PrEP to identify top design candidates: a dissolving microneedle patch (MNP) for local (vaginal) delivery and a hydrogel MNP for systemic delivery via the skin. MNPs for local and systemic delivery of rilpivirine were selected for further research and development, and Queens University Belfast (QUB) was identified as a developer of innovative MNP technology for both candidate patches. During Year 4 of HealthTech, the team developed vaginal applicator prototypes and initiated market research in South Africa. We are also in the process of establishing a subagreement with QUB to study delivery of rilpivirine by MNPs.

HealthTech completed initial development and design of applicator prototypes for vaginal delivery of a dissolving MNP. These designs will be used to aid market research activities in South Africa. The iterative design development process included multiple group brainstorming sessions to generate initial broad concepts and refinement of designs through critique by experts (commercialization, public health, microbicide delivery, midwifery, engineering, industrial design, and technical development experts). Ultimately, six vaginal applicator designs that incorporate key required characteristics were selected and prototyped. These initial designs were presented to the United States Agency for International Development (USAID) in July 2015.

Through a competitive bid process, the market research organization Added Value was selected in June 2015 to initiate market research activities in South Africa. Added Value will meet with health care providers and potential users to assess reactions, perceptions, potential acceptability, and concerns or obstacles for future use of patch product concepts for long-acting delivery of HIV PrEP. In September 2015, the subagreement with Added Value was initiated, and we held a project kickoff meeting at the Added Value office in Johannesburg, South Africa. Activities at the meeting included finalization of focus group discussion guides and agreement on project logistics, timeline, and communication strategy. Data collection is scheduled to take place October 12 through 30, 2015 and will include in-person interviews as well as an online data collection platform.

Efforts are under way to develop an agreement with QUB in order to initiate technical development of MNPs containing rilpivirine, including formulation characterization and in vitro drug delivery studies. To this end, PATH is negotiating a three-way materials transfer agreement (MTA) between Janssen Pharmaceuticals (the manufacturer of rilpivirine), QUB, and PATH, as well as a subagreement with QUB

to conduct the rilpivirine MNP technical development. Regular communication and weekly meetings have helped drive the process forward, and final agreements are anticipated by the end of December 2015.

Achievements in Year 4

- Completed prototyping and iterative refinement of applicator concepts for vaginal delivery of a dissolving MNP and presented them to USAID.
- Completed a design brief summarizing the applicator development process and outcomes.
- Created physical prototypes for use in market research focus groups.
- Developed a request for applications and selected a market research organization, Added Value, to conduct user research in South Africa.
- Conducted a project kickoff meeting with Added Value in South Africa to finalize the focus group discussion guides for potential users and health care providers, concept descriptions, and project plan.

Problems encountered and actions taken

PATH continues to be engaged in the negotiation of agreements with QUB and Janssen Pharmaceuticals to enable study and development of MNPs for the delivery of rilpivirine. Given that rilpivirine is not a generically available pharmaceutical agent, it must be directly sourced from Janssen Pharmaceuticals and has required the negotiation of an MTA. While typically not complicated, in this circumstance, the requirement to negotiate a three-party agreement has slowed the MTA process. We believe we are close to reaching terms with both QUB and Janssen on this MTA, and we are preparing to engage in what we hope will be a final round of negotiations on this front.

The subagreement between PATH and QUB to conduct the study has been drafted and is currently under negotiation, but it also involves a third party. QUB has a partnership with a manufacturer, which impacts rights related to their MNP technology; as such, QUB has been seeking approval with this party to agree to certain terms in the subagreement before they proceed.

Pathway from research to field implementation and use

The HealthTech project activities are designed to investigate the feasibility of alternative delivery systems for the use of long-acting rilpivirine for HIV PrEP. In HealthTech Year 3, we developed a draft target product profile, identified the most promising alternative delivery methods, and developed a preclinical product development plan. In HealthTech Year 4, we developed vaginal applicator concepts, created physical prototypes, and initiated market research in South Africa to understand potential user and health care provider perceptions and potential acceptability of the new technology for delivery of HIV PrEP. Pending future support, in HealthTech Year 5, we will initiate preclinical development to determine initial technical feasibility of delivery of rilpivirine by MNP for HIV PrEP. A new activity for HealthTech Year 5 involves technical evaluation and design requirements/concepts for an applicator for RTI's thin-film polymer device for HIV PrEP.

Amoxicillin Dispersible Tablets

Goal

To facilitate improved adherence to amoxicillin dispersible tablet (DT) treatment for childhood pneumonia through the development and evaluation of a job aid (JA) and user-friendly product presentation (PP), and to leverage progress in childhood pneumonia treatment to improve the use of amoxicillin DT for other indications such as neonatal sepsis and possibly severe acute malnutrition.

Status of the project as of September 30, 2015

The project has successfully integrated PATH's work streams in pneumonia and neonatal sepsis, documenting the use of amoxicillin DT for both indications. Through a design meeting hosted in May 2015, we were able to finalize the designs for the global level and then develop a system for creating country- and region-specific versions. French West African and Bangladeshi versions have been developed.

The preparation work for the field evaluation in Kenya has been initiated, with an expected study kick-off in January 2016. PATH has aligned our activities with other partners working in Kenya. PATH also has identified and is contacting the key stakeholders needed to understand and assess introduction points. Next steps for the project include obtaining appropriate ethical permissions, conducting the field evaluation, and sharing results with the United Nations Children's Fund (UNICEF), US Agency for International Development (USAID), amoxicillin DT manufacturers in Kenya, and the Kenya Ministry of Health.

Achievements in Year 4

- Identified overlapping work streams for each indication and sought opportunities to apply lessons learned from the Diarrheal Diseases and Pneumonia Working Group, Injectable Antibiotics Technical Resource Team, and demonstration sites.
- Conducted a scoping analysis to understand progress regarding the adoption and implementation of neonatal sepsis treatment guidelines and to define the need for new or revised resources in Bangladesh.
- Hosted a meeting in New York City on May 28, 2015, with representatives from Dalberg's Design Impact Group, McCann Health, Novartis, Abt Associates/Strengthening Health Outcomes through the Private Sector, Clinton Health Access Initiative, Population Services International, Results for Development Institute, Systems for Improved Access to Pharmaceuticals and Services, UNICEF, and USAID. Completed all revisions of the PP and JA and disseminated to meeting participants and other stakeholders in August 2015. No additional requests for changes were received.
- Identified key governmental and nongovernmental partners involved in amoxicillin DT planning and procurement. Interviewed representatives from all target countries and Nigeria on their approach to the scale-up of amoxicillin DT. Documented timelines and key actors in each country with which to engage regarding the use of the PP and JA.

- Facilitated conversations with manufacturers under consideration for UNICEF Expert Review Panel II approval for amoxicillin DT and manufacturers interested in producing amoxicillin DT to understand the willingness as well as the barriers to incorporating the PP into current packaging.
- Conducted site visits to health care facilities in Homa Bay, Kenya, that are using amoxicillin DT. Met with key administrators to obtain approval for study activities and also with providers to understand how amoxicillin DT is currently dispensed as part of ongoing Kenya Medical Research Institute (KEMRI)-UNICEF operations research. Obtained samples of current amoxicillin DT packaging and Kenya Medical Supplies Authority tablet envelopes to assess and prepare amoxicillin DT packaging for evaluation.
- Finalized the protocol and data collection tools in collaboration with the study team in Kenya and submitted for review by local ethical review board.

Problems encountered and actions taken

The pilot evaluation was unable to move forward in Malawi as originally planned. This prompted our team to explore other options and identify Kenya as an alternative. We were able to find suitable implementing partners and secure approval from other necessary stakeholders (i.e., UNICEF and KEMRI) working in Homa Bay, Kenya.

Pathway from research to field implementation and use

Project activities are designed to facilitate improved adherence to the treatment of childhood pneumonia by providing health care providers and caregivers with necessary resources and clear instructions for the preparation, administration, and use of amoxicillin DT. The need for a user-friendly PP and a JA was assessed (under separate funding) through a landscape analysis of current packaging and user instructions for childhood pneumonia in Year 2. This needs assessment led to the development of design concepts that were tested (under separate funding) with potential end-users in India and Kenya in Year 3. Feedback from potential end-users and national and global stakeholders was incorporated through an iterative design process to generate prototypes of the JA and PP. In Years 4 and 5, the prototypes will be further developed and evaluated through a pilot evaluation. We will also explore synergies between the amoxicillin DT treatment regimen for childhood pneumonia and neonatal sepsis in children under five years old. In addition, we will assess potential introduction points and distribution channels that encourage the uptake and use of these tools. This evidence will be used to develop recommendations for the adoption and implementation of a JA and PP for amoxicillin DT in Kenya that can be applied in other high-burden pneumonia countries.

Chlorhexidine for Umbilical Cord Care

Goal

Coordinate and support efforts to accelerate introduction and global scale-up of chlorhexidine for umbilical cord care in at least ten countries by the year 2016.

Status of the project as of September 30, 2015

The chlorhexidine for umbilical cord care project made excellent progress during the year. Interest in chlorhexidine for umbilical cord care continues to grow and major progress has been made in countries where implementation is under way. Key highlights include the addition of a manufacturer of liquid chlorhexidine in Bangladesh, the addition of a manufacturer of gel chlorhexidine in Kenya (product registration was obtained on November 5, 2015), the addition of two manufacturers of gel chlorhexidine in Nigeria, completion of market research and dissemination of the results in Kenya, stakeholder meetings in several countries, finalization of the introduction and monitoring and evaluation plans for the initial implementation of chlorhexidine in Kenya (program to be implemented early in Year 5), leading the Every Newborn Action Plan (ENAP) coverage task team for chlorhexidine, and leading the chlorhexidine indicator development as part of the larger Newborn Indicators Technical Working Group.

Achievements in Year 4

HealthTech achievements as part of the Chlorhexidine Working Group (CWG)

- Continued the discussion with GlaxoSmithKline (GSK) regarding their go-to-market strategy and focus countries as the back-up supplier so CWG's effort to establish local production and GSK's effort will be effectively leveraged to increase access to 7.1% chlorhexidine digluconate for umbilical cord care.
- Participated in the stakeholder meeting in Nigeria in September 2015 to discuss a national scale-up strategy. HealthTech presented the market research results in the meeting to contribute to the discussion. We will continue to provide support to the Center for Accelerating Innovation and Impact's work to grow the global market for chlorhexidine through a focus on increasing uptake in the private sector.
- Completed market research in Kenya and presented the results to the Newborn Technical Group led by the Kenya Ministry of Health (MOH) in May 2015. The results from the market research showed an even split between gel and solution among women, which helped the Kenya MOH decide to include both gel and solution in their policy and clinical guidelines. The market research results also contributed to development of the core service delivery and communication strategies for the introduction effort in Kenya.
- Developed the introduction and monitoring and evaluation plans to introduce the chlorhexidine product in ten counties in Western and Nyanza regions in Kenya in support of Kenya's MOH effort to

implement the product in their essential newborn care program. HealthTech will begin the introduction in Year 5, leveraging APHIA*plus* project sites.

- Contributed to the development of standardized information, education, and communication materials and health worker orientation package in Kenya, which will also be used in the introduction project in the ten countries in Western and Nyanza regions.
- Leveraging the United Nations Commission on Life-Saving Commodities funding, HealthTech and the United States Pharmacopeia (USP) selected appropriate manufacturers for production of the chlorhexidine product in Kenya. One of the manufacturers, Universal Corporation Ltd., received the provisional approval for its chlorhexidine gel product at the end of June 2015 (they subsequently received the official approval for the product early in Year 5) and initiated stability tests for their chlorhexidine solution. Another manufacturer, Regal Pharmaceuticals, initiated stability tests for both gel and solution chlorhexidine products. USP will continue to provide technical assistance to Universal Corporation and Regal Pharmaceuticals, using its Promoting the Quality of Medicines in Developing Countries project (PQM) funding.
- Initiated and facilitated discussion among key stakeholders in Pakistan to determine the optimal way to establish product supply. Subsequently, USP used PQM funding to visit Pakistan to assess potential manufacturers and hold discussions with the Drug Regulatory Authority of Pakistan in March 2015. USP will continue to provide technical assistance to establish local production in Pakistan.
- Facilitated USP's assessment of ongoing assistance to a chlorhexidine manufacturer in Bangladesh in December 2014. The USP's technical assistance resulted in the registration of the product in the country in the summer of 2015.
- Continued to monitor USP's development of a gel monograph for 7.1% chlorhexidine digluconate for umbilical cord care. The draft monograph is currently posted for public comment and will be finalized early in Year 5.
- Provided feedback to the United Nations Children's Fund Supply Division to facilitate their upcoming tender for both gel and liquid chlorhexidine for umbilical cord care.
- Convened regular biweekly teleconferences with the CWG as well as regular face-to-face meetings. The most recent face-to-face meeting occurred in April 2015.
- Secured CWG partner support to expand resources available in French and support for translation of some resources into Portuguese (for use in Angola, Mozambique, and other Portuguese-speaking countries, as appropriate).
- Revised CWG materials to more effectively communicate safe and appropriate use of chlorhexidine for umbilical cord care.

- Provided technical review of two chlorhexidine for umbilical cord care videos through Medical Aid Films and the Global Health Media Project.
- Revised the country status chart to include regulatory status and ownership to identify potential supply gaps.

Achievements as members of the United Nations Commission on Life Saving Commodities (UNCoLSC) (not funded under HealthTech):

- Participated in a stakeholder meeting with the Mozambique MOH in January 2015, which resulted in the MOH's commitment to move forward with the implementation of the chlorhexidine product. Subsequently, the purchase of 29,000 tubes (25g/each) of gel chlorhexidine was supported to help kick start the product introduction in Mozambique.
- Participated in a stakeholder meeting with the Afghanistan MOH in May 2015, which resulted in gaining a consensus on developing a national strategy for implementation of chlorhexidine for umbilical cord care. The national strategy is currently under development.
- By leveraging HealthTech funding, an onsite rapid assessment and due diligence of five interested manufacturers in Kenya was completed in November 2014 and three companies were selected for further assessment. The report of the onsite rapid assessment was finalized and sent to USAID and the Kenya MOH. Good Manufacturing Practice (GMP) assessments on two out of the three manufacturers were conducted in April 2015. One of the companies, Universal Corporations, received a product registration for its gel product in November 2015.
- Assessed the feasibility of local production in Uganda in October 2014. A final assessment report, which recommended importing the chlorhexidine product, has been completed and was shared with the MOH in January 2015.
- Estimated cost for technical assistance in order to aid program implementers to prioritize the most critical activities for their situation. The document was shared at the CWG meeting in October 2014. Using feedback from the CWG, an interactive tool and a graphic were developed.
- Implemented a small study using a manikin to determine dose volume for multiple-day application for liquid and gel chlorhexidine, in the hope that the information from this study will aid ministries of health and manufacturers to make decisions of product volume required for seven-day application.
- Served as Convener of the Newborn Health Technical Reference Team (TRT) under the UNCoLSC (the four commodities under the Newborn TRT are chlorhexidine, neonatal resuscitation devices, injectable antibiotics, and antenatal corticosterioids).
- Reviewed and provided feedback to UNICEF on the newborn health components of the Reproductive Maternal Neonatal Child Health Trust Fund country plans.
- Led the Chlorhexidine Coverage Task Team and the development of feasible chlorhexidine coverage indicators as part of the ENAP Newborn Technical Working Group. This work resulted in a publication

in September 2015. Moxon et al. Count every newborn; a measurement improvement roadmap for coverage data. *BMC Pregnancy and Childbirth*. 2015;15(Suppl 2):S8.

- Provided input and guidance on the UNCoLSC Health Worker Technical Resource Team (TRT) toolkit.
- Continued engagement with the Global Market Shaping, Quality, and Regulation TRT.
- Provided input and guidance on the update to the UNCoLSC's Advocacy Toolkit and the final version of the UNCoLSC Quantification Guide for the 13 Life-Saving Commodities.
- Participated in ongoing engagement with the Digital Health TRT to support chlorhexidine introduction in Kenya.

Chlorhexidine was highlighted in the following publications:

- Inclusion of chlorhexidine for umbilical cord care in over 30 international and domestic newspaper articles and blog posts.
- Inclusion of chlorhexidine for umbilical cord care in the Nigerian National Newborn Health Conference in October 2014.
- Inclusion of chlorhexidine for umbilical cord care in a speech given by US Agency for International Development (USAID) Administrator Dr. Rajiv Shah at the launch of Saving Lives at Birth 2.0 on October 7, 2014.
- Presentation by CWG members titled "Reducing neonatal mortality—prevention, early detection and treatment of infections—experiences from Asia and Africa" at the 14th World Congress on Public Health in Kolkata, India, on February 2015.
- USAID Report to Congress 2014: USAID Health-Related Research and Development Progress Report.
- Presentation by CWG member titled "Chlorhexidine use experience: program and policy implications in sub-Saharan Africa" at Uganda's First Maternal and Newborn Health Conference in Kampala, Uganda, in June 2015.
- A CWG poster and four other chlorhexidine-focused posters from CWG partners were presented at the Global Call to Action Summit in New Delhi in August 2015.
- Chlorhexidine was included in the presentation "Breakthrough innovations to save mothers and children" at the Global Call to Action Summit in New Delhi in August 2015.
- Sinha A, Sazawal S, Pradhan A, Ramji S, Opiyo N. Chlorhexidine skin or cord care for prevention of mortality and infections in neonates. *Cochrane Review*. March 2015. Available at: http://onlinelibrary.wiley.com/enhanced/doi/10.1002/14651858.CD007835.pub2#Survey.

- Walsh S, Norr K, Sankar G, Sipsma H. Newborn cord care practices in Haiti. *Global Public Health*. March 2015; 10(9):1107–1117. Available at: http://www.tandfonline.com/doi/full/10.1080/17441692.2015.1012094.
- Moxon SG, Ruysen H, Kerber KJ, et al. Count every newborn; a measurement improvement roadmap for coverage data. *BMC Pregnancy and Childbirth*. 2015;15(Suppl 2):S8. Available at: http://www.biomedcentral.com/1471-2393/15/S2/S8.

Problems encountered and actions taken

Although GSK stated that they would be a back-up supplier, their target countries for market entry include countries where local pharmaceutical companies are already supplying the chlorhexidine product. The CWG continues to engage in discussions with GSK to guide their efforts so that their resources will be used more effectively to fill gaps in product supply and will result in increased access to medicine globally while supporting capacity development of local manufacturers.

The Ebola outbreak in the Western African region negatively affected the progress of the chlorhexidine introduction and implementation effort in the region. The CWG has already resumed its effort to introduce and implement chlorhexidine after the Ebola outbreak. Discussion on the development of a costed scale-up plan for Liberia, which was on hold due to Ebola outbreak, was reinitiated, and the work will soon begin.

The work in Year 4 underscored the importance of continued, coordinated effort to effectively scale up chlorhexidine in newborn essential care programs. In Nigeria, upon the completion of the USAID Targeted States High Impact Project, there was a concern about which organization would continue to coordinate the scale-up effort and closely work with Nigerian MOH. In Francophone Western African countries, there have been no organizations on the ground who could effectively facilitate the scale-up effort. The CWG discussed these issues with USAID and other CWG partners and continued to press the importance of having coordinating agencies. Eventually, in Nigeria, the Maternal and Child Survival Program and the Clinton Health Access Initiative supported the stakeholder meeting in September 2015, which provided a valuable opportunity to review the effort in the past and discuss next steps among key stakeholders. In Niger, a Francophone African country, John Snow, Inc. decided to take a lead to scale-up chlorhexidine in the country.

The stakeholder meeting being planned for Angola has been put on hold. The CWG had engaged with the director of the Reproductive Health division at the MOH, who has now left due to a very serious health issue. The permanent replacement who can make decisions for the Reproductive Health division has only recently been identified. The CWG reengaged with the Angolan MOH toward the end of Year 4.

The monograph for the gel formulation of 7.1% chlorhexidine digluconate could not be published in the USP–National Formulary since the product will be not be used in the United States. However, USP has now included in the draft monograph a statement about how USP may handle monographs for this and other high-impact drugs that are legally marketed outside the United States. USP continues to explore a potential venue to publish the monograph.

Pathway from research to field implementation and use

The project activities will focus on implementing the chlorhexidine intervention over the course of five years. In Year 1, we will add to the evidence base by strengthening the application to the World Health Organization Essential Medicines List and solidifying the strategy for global rollout by convening stakeholders. During Year 1, the CWG was formalized; this is an international collaboration of organizations committed to advancing the use of 7.1% chlorhexidine digluconate for umbilical cord care through advocacy and technical assistance. The CWG is jointly creating a strategy for chlorhexidine rollout globally. PATH, as the Secretariat of the CWG, will lead the group to identify and coordinate programmatic opportunities for chlorhexidine integration into global and regional platforms as well as build potential supplier bases for regional manufacturing and distribution. In Years 2 and 3, we will also provide leadership and technical support for both supply and demand initiatives in support of the United Nations Commission on Life-Saving Commodities Year 1 implementation work plan. In Years 4 and 5, we will continue to lead this work by building on the knowledge and implementation base to scale the chlorhexidine product worldwide. In addition, we will focus on generating operational data through introduction of the chlorhexidine product in ten counties in Kenya. This operational data, together with development of a national scale-up strategy, which will be concurrently done, will contribute to accelerating the national scale-up of chlorhexidine in Kenya. The process and information that result could also help facilitate national scale-up of the product in other counties.

Cold Chain Equipment Inventories

Goal

To make collecting, updating, and using cold chain equipment inventory (CCEI) data common and sustainable practices among Expanded Programme on Immunization (EPI) teams and their partners through the development and introduction of an appropriate inventory system that makes evidence-based equipment planning and management easier at all levels of the vaccine supply chain.

Status of the project as of September 30, 2015

The cold chain equipment inventories project successfully established a set of important resources and ongoing discussions about the role of CCEI data in immunization supply chain planning and management. A CCEI data standard was drafted based on the work developing and implementing a cold chain equipment manager (CCEM) in collaboration with EPI teams. This draft was refined with technical input from the World Health Organization (WHO) and United Nations Children's Fund (UNICEF). The most recent draft of the CCEI data standard will be posted on TechNet (http://www.technet-21.org/en/) as a reference from the UNICEF Program Division, and will support a set of CCEI template data collection forms intended to help EPI teams and consultants strengthen cold chain equipment management. The CCEM will continue to be implemented by some UNICEF consultants due to its unique functionality for CCEI data management. At the same time, a web-based equipment inventory will soon be released as part of the global DHIS 2 software platform, providing a new tool to help EPI teams collect and use CCEI data.

Achievements in Year 4

- Non-HealthTech funding was identified to support the final development step that will allow the CCEI prototype to be released as an integrated application with the current DHIS2 software.
- Worked with DHIS2 developers in India to review the CCEI module implementation plan and finalize the documentation of use cases and software requirements.
- Submitted a new scope of work for DHIS 2 developers in India to create a set of visualizations and dashboards that illustrate how indicators on equipment working status, repair history, and capacity gap analysis can be developed in DHIS 2.
- A poster and presentation on the rationale and content of equipment inventory and temperature monitoring data standards were presented in breakout sessions at the TechNet 2015 conference.
- CCEI Data Standard definitions for cold chain equipment functional status and identification were used in the Gavi, the Vaccine Alliance supply chain dashboard guidance document.
- CCEI data collection forms informed by the work of this project will be posted by UNICEF on the TechNet website at the end of 2015. This is a step toward formalizing a data standard for cold chain equipment inventories under the logos of UNICEF and Gavi.

- With non-HealthTech funding, PATH drafted a concept note on behalf of the Ghana Health Service to request support to deploy the DHIS 2/CCEI module as an integrated component to their national health information management system.
- Worked with the Malawi EPI team and a UNICEF EPI consultant to successfully enter data into CCEM. This data was used by the EPI team to prepare a Gavi health system strengthening application.
- Responded to a request for assistance from the UNICEF Pakistan Polio Team as they look to customize CCEM for subnational manager requirements.
- Met with the team supporting the Better Immunization Data Initiative project in Zambia to review an existing cold chain equipment inventory dataset and to share information from discussions in 2013 with the WHO and EPI teams in Zambia on their interest in deploying CCEM.
- Met with John Snow, Inc. and the Ministry of Health in Pakistan who have now integrated the CCEM data model into the Vaccine Logistics Management and Information System software program funded by the US Agency for International Development.
- HealthTech responded to technical questions from UNICEF South Sudan and UNICEF Somalia, which are looking to conduct cold chain equipment inventories with the CCEM tools in 2016.

Problems encountered and actions taken

While many of the strongest EPI teams are able to initiate data collection and use CCEM independently, this process takes a significant amount of effort, time, and funds. Often, additional support from a consultant can help overburdened EPI teams with this process. Additionally, EPI teams are often required to respond urgently to sudden funding opportunities. The web-based CCEI application in DHIS 2 will ideally provide many EPI teams with a tool that can support routine and ongoing use and updating of CCEI data. This will ensure that these data remain accurate and can be accessed whenever needed by national logisticians or district-level managers.

PATH proposed a collaborative agreement with UNICEF to help access additional resources to support customization of the CCEI application in DHIS 2 to country requirements. Efforts were also made to help the Ghana Health Service secure modest resources to integrate the CCEI application with their national DHIS 2 Health Information Management System. However, neither of these efforts to take the DHIS 2 CCEI application forward to implementation in a first country was successful. UNICEF is currently in working with the DHIS 2 development team in Oslo to scale up the CCEI application in Laos.

Pathway from research to field implementation and use

The current CCEM software tool supports EPI and partners in the management of a national CCEI and functions as an equipment-planning tool for national-level EPI managers and global immunization experts. However, to make implementation and use of CCEI data common and sustainable practices by EPI staff at all levels of the vaccine supply chain, we must make assess to inventory data and tools easier for staff at lower levels. In Year 2, we will engage in a set of focused needs assessments to identify the information requirements of cold chain managers at subnational supply chain levels. In Years 2 to 3, we will use the assessment outputs to help develop, test, and demonstrate simple and appropriate tools that

can integrate with the current CCEM tool but make CCEI data available to inform decisions by lower-level cold chain managers. We will also continue to refine the existing CCEM tool to make it simpler to use as a national-level planning and management tool. Throughout Years 1 through 5, we will continue to support EPI teams in CCEI data collection and use for decision-making at all levels of the vaccine cold chain. As part of ongoing CCEM implementations, we will develop, test, and refine a set of training materials and develop regional CCEM expertise, in collaboration with partners, to create a sustainable set of technical resources that can increasingly support CCEM use beyond this project.

Fast-Dissolving Tablets for Microbicide Delivery

Goal

Demonstrate technical feasibility of developing low-cost fast-dissolving tablet (FDT) dosage forms of tenofovir (TFV) using freeze-drying technology.

Status of the project as of September 30, 2015

During the early phase of the project, the technical activities focused on screening multiple TFV FDT formulations with varying sugar, polymer, and bulking agent compositions to down-select the lead TFV FDT candidate for further evaluation. The screening of the TFV FDTs was based on evaluation of physicochemical and handling properties, moisture content, disintegration time in simulated vaginal fluid, and characteristics (texture, insoluble) post-disintegration. Based on the results, TFV FDT candidates Micro-001 and Micro-006 were selected for stability evaluation under elevated conditions of temperature and relative humidity at (±40°C/±75% relative humidity) as per International Council for Harmonisation guidelines.

Currently, Micro-001 FDT contains a complete dose of TFV at 40 mg (per tablet) and is undergoing stability evaluation at CONRAD in a controlled humidity chamber. The TFV FDTs are in primary polyvinyl chloride blister packaging with secondary aluminum foil packaging. At select time points, the FDTs are evaluated for potency (conducted at Thomas Jefferson University), moisture content, and disintegration. The three-month stability study results indicate the moisture content is less than 2.5%. Tablets can be dissolved within 30 seconds.

Achievements in Year 4

- PATH and CONRAD selected one lead and one back-up TFV FDT candidate for in vitro evaluation and a long-term stability study.
- Conducted a cost of goods analysis on TFV FDTs prepared via the freeze-drying approach.

Problems encountered and actions taken

- Due to the disappointing results of the TFV 1% gel clinical study, as per US Agency for International Development guidance, the PATH FDT team will not pursue additional TFV FDT activities with in Year 5. In response and in collaboration with USAID, the PATH team then established relationships with both the Population Council and Scrips Research Institute and developed workplans to evaluate the feasibility of formulating their respective microbicide compounds as FDT's. This will allow the team to leverage the TFV FDT work with these alternative compounds during Y5.

Pathway from research to field implementation and use

The project activities over the one-year time period are focused on evaluating the FDT technology as a potential platform for local delivery of microbicides for HIV prevention. During this time frame, separate

solid dosage forms in an FDT format, incorporating either the HIV-inhibitor griffithsin or broadly neutralizing antibodies, will be designed and developed using a freeze-drying approach.

Innovation Countdown 2030

Goal

Identify, evaluate, and raise awareness of technologies and ideas sourced from the global community that can accelerate progress and "bend the curve" by dramatically accelerating progress toward achieving the United Nations 2030 Sustainable Development Goals (SDG) health targets.

Status of the project as of September 30, 2015

Reimagining Global Health, the Innovation Countdown 2030 (IC2030) inaugural report, features 30 high-impact innovations selected by independent global experts; health impact modeling results, and commentaries by ten health, technology, and business leaders around the world informed the selection. The report is available at ic2030.org. The report was officially launched on July 13, 2015, at a standing-room-only, official side event at the United Nations (UN) Financing for Development meeting in Addis Ababa, Ethiopia. The event was co-hosted by PATH, the Bill & Melinda Gates Foundation, Government of Norway, United Nations Foundation, and Grand Challenges Canada. It engaged a cross-sector audience of 70 people in a discussion around the report, including how we can keep health innovations cost-effective and how we can ensure investment is made in the innovations with the most potential impact.

PATH has received positive feedback on the value of the IC2030 outputs and how they are being used in various high-level discussions to spur dialogue around investment in innovation from groups including the World Bank, Philips, UBS, the Global Health Investment Fund, and others. There is a strong interest in our vetted methodology, especially the health impact modeling. The Becton, Dickinson and Company Executive Team, which includes the chief executive officer of the company, invited PATH to present its vetted methodology at a teleconference in September 2015. It is discussing additional ways to engage with PATH around this work. At the United Nations Foundation Summit, IC2030 health impact modeling results were used by an entrepreneur to pitch her technology. Grand Challenges Canada invited PATH to present at an innovation curation workshop in Toronto. Inquiries about the work generated from IC2030 continue to come in, as do discussions about Phase II with potential future partners and donors.

Achievements in Year 4

- The online survey that was developed and launched resulted in over 500 ideas from 46 countries. About 30 percent of innovation submissions were from people in low- and middle-income countries. The majority of submissions came to us through the survey from a broad spectrum of experts including technology developers, health leaders, academics, industry experts, investors, donors, and nongovernmental organizations. (Select innovations were also included from Saving Lives at Birth 2014 and Grand Challenges Canada.)
- The qualitative assessment methodology generated and vetted with eight external advisors during the summer of 2014 was used to reduce more than 500 innovations to a more manageable number (175) of candidates using a stoplight framework. Data entry and quality control of innovation submissions

were conducted. Information from the assessment methodology also informed the quantitative impact modeling of maternal, neonatal, and child health innovations.

- A quantitative methodology to assess maternal, neonatal, and child health innovations was developed. Disease area models were generated for eight maternal, child, and neonatal health innovations. The models estimated lives saved, percent reduction in deaths, and intervention and downstream costs between 2015 and 2030. The modeling results were presented in the inaugural IC2030 report *Reimagining Global Health.*
- The external selection process successfully identified 30 promising innovations and engaged over 60 thought leaders around the world. First, eight panels of independent experts organized by health area ranked the innovations. Health areas included maternal health, child health, neonatal health, reproductive health, HIV/AIDS, tuberculosis, malaria, and noncommunicable diseases. Second, an interdisciplinary, independent expert panel was engaged to conduct the final ranking. Rankings were based on what each panelist believed has the most promise to accelerate progress toward the SDG health targets, the innovation definitions provided, and the panelists' broader contextual knowledge of global health.
- An interactive data visualization tool was created with Tableau Software Company to showcase more than 170 innovations that were submitted for consideration by our expert panels. The tool can be used to create custom views of innovations for specific diseases, populations, platforms, and stages of development. See http://ic2030.org/visualization.
- The report has been downloaded over 5,000 times as of September 15, 2015. See ic2030.org for updated content, including the data visualization tool.
- Videos on the report were created by PATH, and a PATH-led partner press release was distributed.
- Media coverage of IC2030 and the *Reimagining Global Health* report includes 18 media placements, of which 10 stories reached high-priority audiences, such as those of Tech/*Business Insider*, Devex, *The Guardian*, *Huffington Post*, National Public Radio, *Stanford Social Innovation Review*, Smithsonian.com, and Voice of America. PATH also contributed to a *Huffington Post* series on SDGs and a live question-and-answer event on *The Guardian* around innovations needed to revolutionize global health by the year 2030.
- Digital coverage includes over 1,300 #IC2030 tweets that were delivered 8.3 million times and reached over 3.7 million Twitter users; this included partner promotion of PATH's infographics and videos. On Facebook, 24,000 views of PATH's IC2030 videos were delivered to 66,000 people.

Problems encountered and actions taken

No problems were encountered.

Pathway from research to field implementation and use

In Year 1 (HealthTech Year 4), we will focus on developing a survey to gather information on innovations as well as creating a methodology for prioritizing these innovations. An external selection process with outside experts will determine a list of 20 to 30 innovations to showcase in the final report. The final report will be disseminated in July 2015 at the UN Financing for Development conference in Ethiopia, along with an expanded version of the IC2030.org website. Continued communications activities will be conducted to promote the report's findings, stimulate global dialogue, and drive traffic to the website. Preparatory work for Year 2 of IC2030 will begin after the launch of the final report. Should additional funding become available in Year 2 (HealthTech Year 5), we will continue by tracking showcased innovations through case studies and highlighting real-time progress and challenges in advancing these innovations. In addition, further analysis on the importance of system innovations will be pursued. Furthermore, we will source additional innovations, focusing on health areas that received fewer nominations in the first year, (i.e., noncommunicable diseases). Health impact modeling will be conducted for innovations in other health areas beyond maternal/child/newborn health. We will more proactively partner with organizations that can help source innovations from around the globe, including universities located in developing countries and the US Agency for International Development's Center for Accelerating Innovation and Impact and Global Development Lab. Finally, we will continue to highlight key insights and themes from our work to raise awareness and stimulate global dialogue about the importance of investing in promising innovations to meet the SDG health targets.

Initiative for Multipurpose Prevention Technologies for Reproductive Health (86% of the funding for this project is pass-through to the Public Health Institute)

Goal

Advance the development of and access to multipurpose prevention technologies (MPTs) that will simultaneously prevent pregnancy and/or sexually transmitted infections and/or reproductive tract infections.

Status of the project as of September 30, 2015

In fiscal year 2014, the Initiative for Multipurpose Prevention Technologies (IMPT) expanded its funding base with the support provided to CAMI Health from the National Institutes of Health Office of AIDS Research (NIH OAR), in addition to ongoing funding from the Bill & Melinda Gates Foundation (BMGF). Support from NIH OAR is building upon some of the IMPT's work on facilitating the MPT scientific agenda (Strategic Area 2). Support from BMGF co-funds CAMI Health's activities as Secretariat for IMPT (Strategic Area 2) and facilitates the MPT scientific agenda. The activities under the third IMPT strategy, conduct MPT communications and advocacy, are not supported under the BMGF funding. These activities are carried out by PATH/HealthTech, the Guttmacher Institute, and Association of Reproductive Health Professionals in conjunction with CAMI Health and IMPT partners.

CAMI Health, hereby referred to as IMPT Secretariat, in collaboration with IMPT partners, made substantial advances in all three of the strategic areas in fiscal year 2014. The IMPT Secretariat and partners highlighted MPTs at a number of important conferences and forums around the world. The IMPT Secretariat staff also responded to requests from IMPT partners for the development of new MPT online resources and materials. The IMPT Secretariat and Steering Committee developed recommendations on high-priority areas for action and follow-up for the MPT field after an iterative development and vetting process. The Scientific Agenda Working Group updated the MPT product pipeline database and, in conjunction with the IMPT Steering Committee and Supporting Agency Collaboration Committee (SACC), strategized around and addressed the identified high-priority issues for the MPT field. Lastly, the Communications and Advocacy Working Group expanded outreach with key stakeholders in the United States, began implementation of key communications messages in Kenya and South Africa, and developed outreach efforts to reach a broad array of experts and stakeholders across the family planning, sexually transmitted infection (STI), and HIV arenas.

Achievements in Year 4

- The IMPT Secretariat finalized the *MPT Investment Tracking Summary* for 2013 data in October 2014.
- The IMPT director participated in the Reproductive Health Supplies Coalition (RHSC) Membership Meeting in Mexico City on behalf of the IMPT in October 2014; awareness-raising activities included

distribution of MPT materials and over one dozen formal and informal meetings with RHSC members about MPTs. These activities resulted in engagement of RHSC members, including United Nations Population Fund representatives and the IMPT Network of Experts, and collaboration among RHSC members on upcoming grant proposals in support of IMPT activities.

- PATH organized and facilitated the Communication Advisory Committees in Kenya and South Africa to develop key MPT messages for Kenyan and South African target audiences and drafted a PowerPoint presentation and a fact sheet to communicate these messages. The South Africa MPT fact sheet was distributed at the Research4Prevention conference in October 2014 and a national maternal child health and nutrition event that took place on December 8–9, 2014. The South Africa fact sheet and message framework and the Kenya PowerPoint presentation are online on the IMPT website's resource center.
- The IMPT Secretariat hosted a biannual joint IMPT Steering Committee and SACC webinar in November 2014.
- The IMPT Secretariat sent requests for review of IMPT priorities for 2015 to the IMPT Steering Committee and SACC in November 2014. Secretariat staff completed data collection for the 2015 IMPT Priority Issues Survey and convened a neutral IMPT review committee to analyze the survey data. A summary of the IMPT high-priority issues identification exercise was finalized and posted on the IMPT website in May 2015.
- The IMPT Secretariat hosted a webinar by Ipsos Healthcare on their study on MPT market demand issues in November 2014.
- The IMPT director authored an article published online in *The Guardian* on December 1, 2014, titled "Can you imagine a world without condoms for safe sex? Scientists can." She also authored an article published online in *RH Reality Check* on December 1, 2014, titled "The need for broad-spectrum STI and pregnancy prevention methods is clearer than ever."
- A special supplement on MPTs was published by the *BJOG: An International Journal of Obstetrics and Gynaecology* in December 2014. The supplement was edited by an IMPT Steering Committee member at the World Health Organization, in collaboration with the IMPT director. Included were two articles co-authored by IMPT Secretariat staff. The IMPT Secretariat released a press release and has distributed the journal issue to stakeholders, including shipping over 300 hard copies.
- The IMPT Secretariat completed the *MPT Funding Enhancement and Optimization Strategy* in January 2015 and leveraged funds from the BMGF to develop a more focused strategy for engaging European funding groups in the IMPT and larger MPT field.
- The IMPT Secretariat posted and disseminated a press release on the FACTS 001 [Follow-on African Consortium for Tenofovir Studies] trial results in February 2015.
- The IMPT Secretariat began the process of a comprehensive update to the MPT Product Development Pipeline Database in March 2015. This update was completed in June 2015. An MPT pipeline

summary and inclusion/exclusion criteria for the database were posted on the IMPT website in July 2015.

- The IMPT contractor Guttmacher Institute briefed the Friends of NICHD, a Washington, DC–based coalition of advocates in support of the National Institute of Child Health and Human Development (NICHD), on the need for MPTs. As a result, the coalition included MPTs in the fiscal year 2016 funding for NICHD.
- The Guttmacher Institute briefed the International Family Planning Coalition, a Washington, DC–based coalition of advocates in support of US government funding for international family planning efforts, on the need for MPTs. The International Family Planning Coalition requested language in support of research and development for new MPTs and contraceptives in their request for funding in fiscal year 2016.
- The IMPT director met with staff from the office of the US Global AIDS Coordinator in April 2015 to discuss MPTs; the linkages between HIV and sexual and reproductive health broadly; the Determined, Resilient, Empowered, AIDS-free, Mentored, and Safe (DREAMS) initiative for adolescent women and young women; and hormonal contraceptives and HIV.
- The IMPT Secretariat convened a roundtable on commercialization and social-behavioral issues for MPT development in March 2015 in Bethesda, Maryland, in conjunction with a Microbicide Trials Network meeting. The roundtable summary was circulated in June 2015 and is also available on the IMPT website.
- An Sexually Transmitted Infection Working Group member/IMPT scientific advisor presented on MPTs at an STI Clinical Trials Group meeting in Washington, DC, in April 2015.
- The IMPT Secretariat, in collaboration with the RHSC, NIH OAR, and US Agency for International Development (USAID), organized a Spanish-language webinar on MPTs for the Latin American and Caribbean region in May 2015. This webinar had nearly 60 participants from over six different countries in attendance.
- As part of the implementation process for the MPT funding optimization and enhancement strategy, the IMPT Secretariat, in collaboration with key consultants, developed a messaging document to educate and engage new funding agencies around MPTs in May 2015.
- In May 2015 in Rockville, Maryland, the IMPT Secretariat organized an in-person meeting on hormonal contraceptives in MPTs as a follow-up to the September 2014 meeting on hormonal contraceptives in MPTs. Secretariat staff distributed the meeting report in September 2015.
- The IMPT Secretariat organized an in-person meeting to jointly convene the IMPT Steering Committee and SACC in Washington, DC, in June 2015. Secretariat staff posted the meeting summary and distributed the full meeting report to Steering Committee members in September 2015.
- The IMPT Secretariat hosted an in-person executive convening of the SACC in June 2015 in conjunction with the joint IMPT Steering Committee/SACC meeting in Washington, DC. The

summary of this meeting was posted on the IMPT website and the full report was distributed in September 2015.

- The IMPT Secretariat finalized the MPT target product profile technical brief and product-type-specific target product profiles for the long-acting injectable and intravaginal ring in June 2015. These are posted on the IMPT website.
- The IMPT Secretariat finalized data collection for 2014 investments in June 2015 in collaboration with AVAC. A final MPT investment tracking report has been drafted and will be included as part of the IMPT annual report to be released in January 2016.
- The IMPT Secretariat began initial planning for a technical convening on MPT clinical evaluation and trial design; the convening is slated for spring 2016 to address high-priority questions for the MPT field that were identified in the 2015 IMPT Priority Issues Survey. An in-person planning meeting for this technical meeting was held in June 2015, with follow-up teleconferences in June and September of 2015.
- IMPT Secretariat staff briefed the Elizabeth Glaser Pediatric AIDS Foundation and the Norwegian Embassy in Washington, DC, on MPTs in June 2015.
- The South Africa fact sheet was updated to reflect relevant microbicide trial outcomes, and 200 copies were distributed at the South African AIDS Conference in June 2015.
- The Guttmacher Institute published a policy brief in September 2015 on making the investment case for MPTs.
- The IMPT Secretariat staff wrote two articles for publication in the Indian Society for the Study of Reproduction and Fertility newsletter's special issue on MPTs, which were circulated in September 2015.
- The IMPT Secretariat, in collaboration with the World Health Organization and the University of California, San Francisco, coordinated an MPT panel focusing on STIs at the International Society for Sexually Transmitted Diseases Research World STI & HIV Congress in Brisbane, Australia, in September 2015.
- The IMPT Secretariat distributed a press release, in partnership with the Bixby Center, on the MPT panel at the International Society for Sexually Transmitted Diseases Research conference in Brisbane, Australia, in September 2015.
- The IMPT Secretariat held two stakeholder teleconferences in the summer of 2015 to solicit feedback for the *Commercialization and Social-Behavioral Framework for MPTs*. The framework, renamed the IMPT *Market Access framework*, is currently being finalized. A companion workbook to operationalize this framework among MPT product developers and funders is currently being developed in collaboration with USAID's Accelerating Innovation and Impact team.

- The IMPT Secretariat finalized the structure for the new, user-friendly MPT resource center on the CAMI Health website, which will be launched in Quarter 1 of Year 5.

Problems encountered and actions taken

No problems encountered

Pathway from research to field implementation and use

The IMPT is a global coalition with the goal of advancing the development of MPTs for reproductive health. The IMPT will advance development of MPTs over the next five years through the following key initiatives: developing a scientific agenda for MPT research and development, including a sociobehavioral research component that will guide prioritization of investment and product development; expanding global support for MPT development, including among supporting agencies, researchers, and advocates both within and outside of the United States; and fostering greater coordination and collaboration among key stakeholders involved in MPT development. These activities will be carried out simultaneously in Years 1–5, with the goal of increasing the global MPT product development pipeline by Years 4 and 5.

Injectable Antibiotics for Newborn Sepsis Treatment

Goal

Contribute to efforts to accelerate availability, accessibility, and correct use of injectable antibiotics for newborn sepsis treatment in key countries by the year 2016.

Status of the project as of September 30, 2015

PATH continues to participate in the United Nations Commission on Life-Saving Commodities (UNCoLSC) Injectable Antibiotics Working Group. PATH is responding to expressed project needs, providing feedback, and sharing information with UNCoLSC and other partners and stakeholders. Several activities have been completed, and others await further decision-making from the World Health Organization (WHO)/UNCoLSC Injectable Antibiotics Technical Resource Team (IA TRT).

Achievements in Year 4

- Participated in the IA TRT in-person meeting in Washington, DC, in October 2014.
- Provided detailed feedback to the Uganda injectable antibiotics/neonatal sepsis bottleneck analysis in March 2015.
- The landscape of alternative formulations of gentamicin was completed and reported as a single document along with the landscape of alternative delivery platforms. The landscape, named *Gentamicin for Treatment of Neonatal Sepsis: A Landscape of Formulation, Packaging, and Delivery Alternatives*, was shared with the US Agency for International Development (USAID) on August 4, 2015, for review and feedback.
- The global strategy to support implementation of new WHO guidelines for outpatient treatment of neonatal sepsis was drafted and shared with the IA TRT subgroup in June 2015. We are awaiting final feedback to finalize and share with the rest of the IA TRT.
- A scoping analysis to understand progress regarding the adoption and implementation of neonatal sepsis treatment guidelines in Bangladesh is under way. Existing job aids from early adopter countries were compiled, reviewed, and presented to Save the Children in September 2015. Interviews with implementing stakeholders in Bangladesh have been conducted. Health care provider interviews will be conducted in Bangladesh in November 2015.

Problems encountered and actions taken

Many of HealthTech's specific planned activities are very dependent on the pace of decisions made by the IA TRT and the WHO processes for finalizing and publishing updated treatment guidelines—processes that have taken longer than expected. We've kept in close communication with both parties and have adjusted our workplan activity timing as needed.

Pathway from research to field implementation and use

The project activities will focus on increasing the availability of and access to appropriate injectable antibiotics over the course of three years. In Year 1 (HealthTech Year 3), we will align with the IA TRT

of the UNCoLSC to characterize the manufacturing, use, and quality of the drugs. Concurrently, HealthTech will complement the UNCoLSC work by assisting in the planning of strategies to address bottleneck analysis recommendations and updated treatment guidelines. In Years 2 and 3 (HealthTech Years 4 and 5), we will continue supporting the IA TRT, drive innovative technology and market-shaping approaches related to injectable antibiotics, and support implementation needs. HealthTech will complement the UNCoLSC work in the area of innovation by revising a landscape of current delivery options for gentamicin and investigating the feasibility of alternative routes of administration for gentamicin.

Neonatal Resuscitators

Goal

Conduct an independent, third-party evaluation of new designs of neonatal resuscitators and/or component pieces (i.e., face/device interface) as part of the Helping Babies Breathe (HBB) Global Development Alliance (GDA) to reduce neonatal mortality by improving newborn resuscitation.

Status of the project as of September 30, 2015

PATH continues to participate in the United Nations Commission on Life-Saving Commodities (UNCoLSC) Neonatal Resuscitation Working Group (WG); PATH is responding to expressed project needs, providing feedback, and sharing information with the HBB editorial group, UNCoLSC, and other partners and stakeholders. The HBB GDA has ended and evolved into the Survive & Thrive (S&T) GDA, which PATH is not officially part of. Several reports/tools have been completed and shared with key stakeholders. During this year, one research study was completed and disseminated. In the coming year, one more research study will be completed and reprocessing guidelines for neonatal resuscitation equipment will be finalized.

Achievements in Year 4

- Helped plan and participated in the UNCoLSC Neonatal Resuscitation WG in-person meeting in Washington, DC, in October 2014.
- Reviewed and provided feedback to the HBB GDA final report titled *HBB Lessons Learned Guiding The Way Forward* in April 2015.
- Completed the final report titled *Understanding Production Capacity of Neonatal Resuscitator Manufacturers* in October 2014, which concluded that there is enough manufacturing capacity to meet the estimated market size for the eight UNCoLSC pathfinder countries. The report was shared with the US Agency for International Development (USAID) in November 2014 and with the Neonatal Resuscitation WG members in December 2014.
- Published the article "Performance and acceptability of two self-inflating bag-mask neonatal resuscitator designs" in the journal *Respiratory Care* in September 2015, which reported on the user evaluation of the Upright Resuscitator at Seattle Children's Hospital.
- Completed a fetal monitors guide as part of the series of commercially available technologies related to the S&T GDA. It was shared with the HBB GDA and the Neonatal Resuscitation WG members in January 2015. All the S&T GDA purchasing guides were posted on the PATH and Life-Saving Commodities websites and linked to the Healthy Newborn Network website by June 2015.
- Completed the final report titled *Assessment of Reprocessing Practices for Neonatal Resuscitation Equipment* in June 2015. The study assessed factors affecting adequate reprocessing of bag-and-

mask resuscitators and manual suction devices in Uganda. The report was shared with USAID, the Neonatal Resuscitation WG, and HBB GDA members in July 2015.

- The Reprocessing Consensus Group is led by HealthTech. It was created in July 2015. As of September 30, 2015, HealthTech has facilitated 11 meetings. The reprocessing guidelines for neonatal resuscitation equipment are still being determined and will be finalized in the coming year.
- Completed data collection in Aligarh, Uttar Pradesh, India, in August 2015 for the user evaluation of the Upright Resuscitator with Save the Children. Data analysis was completed. The report has been drafted and will be shared with USAID and the Neonatal Resuscitation WG.
- The landscape report, titled *Neonatal Airway Interfaces*, is being finalized and will be shared with USAID.
- Provided input on the World Health Organization (WHO) technical specifications for neonatal resuscitation devices both on the specifications and procurement sections for neonatal resuscitation devices (bag, mask, suction device). WHO decided not to include manikin specifications in the guidelines, as they are not considered devices. WHO is in the process of finalizing the specifications. Separate manikin specifications are being developed by PATH and will be included in the procurement toolkit.
- Completed version 1 of the Neonatal Resuscitation Commodities Procurement Toolkit and shared with the ministry of health and nongovernmental organization procurement personnel and other program managers in Malawi, Tanzania, and Uganda through technical assistance workshops in November 2014. Version 2 of the toolkit will be updated in December 2015 with the feedback received from Malawi, Uganda, working group requests (e.g., regulatory and customs clearance considerations when importing medical devices), and manufacturer updates. Additionally, more in-depth procurement information that was not included in the WHO technical guidelines will be incorporated into the toolkit to make it a more comprehensive document. Ethiopia and one other country will receive procurement technical assistance in the coming year.
- Activities to disseminate tools generated through HealthTech (Guide to Selection, Quantification Tool, S&T Purchasing Guides) and other tools (Procurement Toolkit) began in June 2015 with requests to post links to additional websites (such as Maternova and Teaching-aids At Low Cost). These activities will be further expanded when version 2 of the procurement toolkit is finalized.

Problems encountered and actions taken

Data collection for the user evaluation of the Upright Resuscitator was delayed due to new India Ministry of Health requirements that had to be met before initiating data collection. As of September 2015, data had been collected and was being analyzed. As of November 25, 2015, the draft report was submitted to Save the Children for review.

- Finalization of the Neonatal Resuscitation Commodities Procurement Toolkit will be delayed. Feedback is being incorporated, but the toolkit cannot be finalized until after the WHO commodity specifications are ready. The date when the WHO specifications will be finalized is still uncertain.
- We have been unable to finalize a date for the procurement technical assistance workshop in Ethiopia. The Ministry of Health in Ethiopia has not responded to recent communications sent to arrange for this. Our PATH Ethiopia office informed us that the end of the year is a busy time for the Ministry of Health and advised us to follow-up in January 2016. If we still do not receive a response, a different country with interest in receiving training will be selected.
- The consensus process to determine the reprocessing guidelines for neonatal resuscitation equipment has been prolonged due to paucity of evidence for the methods commonly used in low-resource settings. Agreement on recommendations when evidence is minimal is being reached by consensus and by seeking external input.

Pathway from research to field implementation and use

Project activities will focus on identifying and evaluating any innovation in this product category over the course of five years. Of immediate interest are the simplified resuscitator designs being developed by Laerdal Medical AS. In Year 1, we will evaluate the Laerdal devices in bench testing. In Years 1 and 2, we will seek funding to conduct independent evaluations of these devices in developed- and developing-country settings. In Years 3 to 5, provided we see favorable results from the independent user evaluations in various settings, we anticipate joining a wider group of partners in integrating the new devices into the existing HBB programmatic platform to achieve global scale. We anticipate that any other product innovation in this category will follow a similar pathway from discovery to field implementation and use. Simultaneously, we will determine the market size and adequacy of supply through development and dissemination of an estimation model and quantification tool that can be applied generically to resuscitation equipment. Data from this model will be shared with manufacturers to encourage them to engage in further product innovation in this space.

Noninvasive Hemoglobin Measurement Tools for Anemia Screening

Goal

To evaluate point-of-care hemoglobin measurement and advance the introduction of noninvasive anemia screening technologies in low-resource settings.

Status of the project as of September 30, 2015

Over the course of Year 4 of the project, the team established a collaboration with researchers at the University of Rwanda College of Medicine and Health Sciences. Study goals, objectives, and study design were agreed upon during a visit to Rwanda by the PATH team in December 2014. A clinical trial agreement (CTA) was signed in July 2015 between three parties: PATH, The University of Rwanda, and Masimo Corporation, the developer of the Pronto noninvasive technology. In early September 2015, the study protocol, consent forms, and data collection tools were approved by 1) the PATH Research Ethics Committee, 2) the Rwanda National Ethics Committee, and 3) the Ethics Committee of the University Teaching Hospital of Kigali (CHUK). A three-day training workshop was conducted by PATH at the University of Rwanda in Kigali during the week of September 1. The training included review of the study materials and ethics clearance documents, demonstration and practice with the HemoCue gravity and wicking methods, and training on the use of the Pronto minisensor for children. This study received clearance to begin on Monday, September 14, 2015, and recruitment and enrollment began immediately. A communication plan was developed and implemented by the PATH team, establishing weekly calls with the researchers in Rwanda. The study team is also in close communication with the product engineering and the product introduction teams at Masimo.

As of the last week of September 2015, enrollment in the study is proceeding smoothly and is on target to reach the sample size needed by the end of 2015. Preliminary discussion about a dissemination meeting that would bring together study partners and experts on anemia has been initiated.

Achievements in Year 4

- Confirmed a study site and research partners in Rwanda.
- Signed a CTA between all parties including Masimo, the developer of the noninvasive hemoglobin screening device.
- Agreed on study objectives and developed a study protocol and data collection tools.
- Received ethics approvals for the study from the PATH Research Ethics Committee and two committees in Rwanda: the Rwanda National Ethics Committee and the CHUK Ethics Committee.
- Completed training of the HealthTech and Rwandan research team on study procedures and hemoglobin measurement tools.
- Launched recruitment and enrollment in the study at the pediatric clinic at CHUK.

Problems encountered and actions taken

Length of time to finalize study documents and approvals: The process of approvals for the study as well as for the subagreement is complex and lengthy. The project involved up to four partners, including the device manufacturer and the CHUK pediatric clinic where study participants were recruited and enrolled. At each step of the process, documents had to be reviewed, revised, and approved by all parties. This was further complicated by the University of Rwanda's lack of familiarity with US Agency for International Development and PATH processes and requirements; therefore, each step took longer than expected. The HealthTech team spent a fair amount of time working through the steps with the University of Rwanda, providing as much support as needed to try and expedite the process. The Rwandan team was extremely responsive and open to the requests.

Clinical study insurance: PATH requires that partners in a CTA obtain clinical trial insurance covering study staff. Once it was established that the study team in Rwanda could not be covered for this particular activity under the university insurance policy, the project was stalled while options were explored. Obtaining an insurance policy for the team in Kigali required considerable effort on all sides. The CTA could not be fully negotiated until this issue was addressed. The legal team at PATH provided assistance, determining the level of coverage that was acceptable. It took some time to get quotes from two companies in Kigali. The quotes were higher than expected so the budget had to be revised and renegotiated, which took additional time.

Delay in starting study procedures: Delays in reaching an acceptable subaward budget and in finalizing the CTA pushed the start of the study in Rwanda back by several months. The delays resulted from discussions over budget constraints and the higher than expected study costs. Higher study costs were partly due to the high cost of clinical trial insurance as well as the higher than expected labor commitment to get the study off the ground. The Rwanda and HealthTech teams were extremely committed to seeing this activity proceed successfully. The University of Rwanda team sees this as an important activity for their department in terms of collaboration, capacity-building, and contribution to anemia research; they were willing to further decrease their costs so that the project could resume. The HealthTech team also revised their budget, cutting down on staff time. Every effort was made to find a quick and satisfying resolution to these issues. Ultimately, there was a delay of only four months. The study has successfully started and is proceeding well.

Pathway from research to field implementation and use

In Years 1 through 3, we evaluated the use of noninvasive devices on pregnant women in Ghana to provide key information needed to optimize the devices and refine the practices surrounding their use. In Year 4, a study will be conducted in Rwanda to evaluate the Pronto with DCI mini™ sensor, a noninvasive anemia screening device, as well as two techniques of blood measurement using the HemoCue device. The results will be shared with in-country stakeholders as well as with the Demographic Health Survey (DHS) country teams for field implementation of a validated hemoglobin measurement tool and technique, for use with children younger than 5 years, during the next DHS. In

Year 5, we will disseminate the results and, if the results are positive, look for implementation opportunities.

SILCS Diaphragm, a Nonhormonal Barrier Method for Contraception and Dual Protection

Goal

Advance the commercialization of the SILCS diaphragm by creating supply and building demand, conducting developing-country assessments to build the value proposition for SILCS introduction, pursuing regulatory approvals, and building evidence for appropriate gels to be coupled with the device.

Status of the project as of September 30, 2015

All activities are in-process and are scheduled for close-out by the end of September 2016. Clinical studies, country assessments, and economic modeling are generating evidence that is being shared with global- and country-level stakeholders through multiple channels to refine the SILCS value proposition for various audiences. This is helping build awareness and generate demand for SILCS, as shown by country inquiries. Production has been validated and supply chain is being established through existing distribution networks. Regulatory approvals have been achieved from stringent regulatory authorities and product registrations are under way in other countries. Market launch in developed and middle-income countries is helping to raise awareness and build confidence about this new product, and also to reinvigorate the market for female barrier methods. Kessel and its distributors now market the Caya® diaphragm in more than 25 countries, with the product expected to launch in additional countries in 2016. HealthTech/Kessel continue to assess market opportunities and seek partnerships for introduction in low- and middle-income countries as resources allow, and while we navigate issues around the contraceptive gel.

Achievements in Year 4

- The two CONRAD clinical studies received all required approvals, and implementation is under way. Both studies are on-target to be completed by August 2016.
    - The Phase 1 postcoital testing study will determine the barrier effectiveness of SILCS used with ContraGel® and SILCS used with no gel, compared to SILCS used with the spermicide nonoxynol-9. Participant enrollment was completed in September 2015. Final participant visits are expected in January 2016, followed by data analysis and reporting.
    - The Phase 1 safety study of SILCS and ContraGel® was initiated in July 2015. By September 2015, 16 women were screened, 8 women completed baseline samples, and 4 women completed test cycle 1.
- HealthTech negotiated agreements with the London School of Hygiene & Tropical Medicine (LSHTM) and the University of Bristol for the SILCS Phase 2 modeling. The US Agency for International Development (USAID) has approved the agreements. The modeling is scheduled to start in January 2016, after the discrete choice experiment data collection in South Africa is complete.
- The LSHTM article "Cost-effectiveness of introducing the SILCS diaphragm in South Africa," was published in the peer-reviewed journal *PLOS ONE.* This article reported on the SILCS Phase 1 model

assessing the hypothetical impact when SILCS is introduced as a contraceptive to address an unmet need for family planning; the article received 200 page views during its first week of posting.

- HealthTech's abstract summarizing results from the SILCS health systems assessments and market research in India and South Africa was accepted at the International Conference on Family Planning. Sharing these results will help raise awareness about the SILCS/Caya® diaphragm among developing-country stakeholders and could lead to partnerships for market introduction.
- MatCH Research [Maternal, Adolescent and Child Health Research] presented summary results from the SILCS health systems assessment on the feasibility of SILCS as a multipurpose prevention technology at the HIV Research for Prevention Convention in October 2014.
- MatCH Research presented results of the SILCS health systems assessment and gel delivery study at the South Africa AIDS Conference in June 2015; about 70 stakeholders attended the satellite session. The SILCS team leader also presented about SILCS design development and introduction activities outside South Africa, and met with the USAID South Africa representative to share updates on the SILCS activities and multipurpose prevention technologies. This gave us an opportunity to gauge interest in SILCS introduction among South African stakeholders.
- HealthTech negotiated an amendment to the MatCH subagreement to cover developing a SILCS policy brief based on the outcomes of the health systems assessment. This policy brief will be used to engage South African stakeholders to build a supportive environment for SILCS introduction in South Africa.
- MatCH Research completed implementation of the SILCS gel delivery study in February 2015. The data have been analyzed and a draft report is being reviewed by HealthTech.
- HealthTech met and shared SILCS information with social marketing organizations and other potential partners, including Marie Stopes International, International Planned Parenthood Federation, and DKT International, and explored interest in future introduction.
- HealthTech staff drafted an article for the Indian Society for the Study of Reproduction and Fertility newsletter. The article provides updates on female barrier methods, with an emphasis on the SILCS diaphragm and Woman's Condom, and implications for multipurpose prevention technologies. The newsletter—focused on multipurpose prevention—was published in September 2015; it has been distributed widely in India.
- Kessel achieved Australian regulatory approval in late 2014 for the Caya® diaphragm and Caya® Gel, and distribution was launched.
- Caya® diaphragm was registered in Malaysia, and a pilot activity was initiated to gauge feasibility of introduction among family planning providers.
- DKT expressed interest in the introduction of the SILCS diaphragm in Nigeria. HealthTech shared reports and tools from the health systems assessments and market research in India, South Africa, and Uganda. DKT is assessing the feasibility of market introduction in Nigeria in 2016.
- HealthTech facilitated communication between Kessel and the Expanding Effective Contraceptive Options (EECO) project regarding the procurement of Caya® diaphragms for Malawi and Zambia. HealthTech also participated as part of the Technical Advisory Group for the EECO project.
- HealthTech coordinated communications for the product launch in the United States in June 2015, collaborating with Kessel, HPSRx (the US distributor for Caya®), CONRAD, USAID, and other key

stakeholders. A HealthTech-drafted blog "*A first in 50 years: how a new diaphragm design made its US debut*" was posted to coincide with the press release; the blog generated more than 3,300 page views within the first two weeks. This led to an additional 123,000 page views of the SILCS subsite where SILCS program activities are described. Media coverage of the Caya® launch in the United States was carried by more than 20 print and online journals between July and September 2015. This helped raise awareness of the Caya® diaphragm among other USAID cooperating agencies involved in family planning service delivery, as well as international partners.

- Kessel presented to the German delegation for the International Organization on Standardization (ISO) in May 2015 to share information about Caya® product specifications. The German delegation briefed the full ISO working group on diaphragms and female condoms in September 2015 in Washington, DC. This is an important step that ensures the SILCS design innovations are accepted by the ISO global standards.
- The production process of the Caya® diaphragm has become more stable as Kessel gained experience with production. The in-process rejection rate declined from a high of over 20 percent in 2013–2014 to about 12 percent during production in 2015. This means a higher yield per batch and lower wastage rate, which translates into lower per unit cost for the diaphragm.
- Kessel gained experience balancing production and inventory control over the two years the Caya® diaphragm has been commercially available and as the market develops. In 2015, Kessel manufactured approximately 30,000 units in separate batches of 10,000. Production planning for 2016 is under way, where Kessel plans for 60,000 units to accommodate additional countries. This includes inventory provided free to clinics and stakeholders to raise awareness.
- Kessel developed new packaging for the ContraGel® contraceptive gel in response to feedback from consumer assessments in India and Nigeria. Kessel identified material for individual unit sachet packets, and a pilot production batch has been packed in the new material. Stability testing is underway to validate this alternative packaging.
- Kessel requested an extension of the PATH/Kessel SILCS licensing agreement (originally signed in 2010) to ensure his authority to manufacture SILCS and enter into distributor partnerships in the future. HealthTech staff and our business consultant have reviewed the agreement and patents and are working on an amended and extended agreement. We expect this to be signed by the end of 2015.
- HealthTech negotiated an agreement between Kessel, PATH, and FHI 360 to transfer Caya®/SILCS diaphragm quality assurance testing protocols and testing supplies and to train FHI 360 to become an independent testing center for Caya® diaphragms. (Training will occur in 2016.)

Problems encountered and actions taken

Kessel refined production process controls to narrow variability and reduce rejection rates, and has made progress over the past year, but reject rate is still a concern. Since most rejections are due to cosmetic issues (white streaks from the colorant), Kessel has started providing these units to clinics and providers as "single-use trial kits" for demonstration. This helps address the need for providers to have free or low-cost samples and also allows Kessel to make use of these units that would have been destroyed. Kessel is exploring additional options to optimize production as Kessel plans for the next stage of production scale-

up. Kessel is evaluating opportunities to combine the spring welding and the over-molding into one machine rather than two separate production processes, which will reduce the amount of time required to produce the Caya® diaphragm.

After a year of trying to raise awareness in Malaysia, the local distributor notified Kessel that he is not the right partner for this product. This was his first attempt to distribute a contraceptive and it was difficult to gain access to the organizations involved in providing family planning services. HealthTech is working with Kessel to access family planning stakeholders in Malaysia, and the current distributor will work with Kessel to identify a different distributor and transfer the registration.

CONRAD and USAID hosted a technical meeting to review mucosal safety issues of products that could be used in the vagina or rectum. The aim of the meeting was to determine if experts felt sufficient evidence exists on either Amphora™ gel (being introduced as part of the EECO project) or ContraGel® for USAID to recommend supporting introduction in countries where women are at risk of HIV. The experts acknowledged that the studies CONRAD is implementing with ContraGel® come close to fulfilling the recommended testing, but currently neither contraceptive gel has implemented all the tests recommended. The experts also acknowledged that women in developing countries currently are at risk of the consequences of unintended pregnancy; they also are at risk from other products currently being used that are not regulated. The experts also acknowledged that risk is relative, and they would not have the same concern if these products were introduced in countries where risk of HIV is not as high as in some countries in sub-Saharan Africa.

This reinforces the urgent need to complete these two clinical studies to assess ContraGel® safety. Recommendations from this consultation could ultimately influence USAID's future support introduction of the Caya® diaphragm with either Amphora™ gel and/or Caya® Gel, and certainly which countries are considered appropriate for SILCS introduction with a contraceptive gel.

Pathway from research to field implementation and use

Project activities focus on advancing the commercialization of SILCS over five years by validating a contraceptive gel for use with the diaphragm in developing countries (ContraGel®, tenofovir, or other gel); conducting developing-country market assessments, cost-effectiveness/health impact assessments, and demonstration studies to assess the value proposition for SILCS both as a barrier contraceptive and a microbicide delivery system for dual protection; and then building strategies for market introduction, developing regulatory submissions, and scaling up production to bring SILCS to key developing-country markets.

Skunkworks

Magnesium Sulfate Dilution Bottle

PATH has adapted the concept of a dilution bottle to simplify the process of magnesium sulfate ($MgSO_4$) administration. The dilution bottle contains a 50% $MgSO_4$ solution and is pre-marked with a fill line. When a 50% $MgSO_4$ solution is required, the necessary amount can be withdrawn directly from the bottle. When 20% $MgSO_4$ is required, a health care worker can simply add sterile water (diluent) to the bottle up to the pre-marked fill line to make a 20% $MgSO_4$ solution. This $MgSO_4$ dilution bottle can facilitate the safe calculation of required doses by obviating the need to remember complex equations for dilution, thus minimizing the chance that the wrong dilution might be administered. This dilution bottle could also reduce the burden associated with procurement and inventory control since only one type of dilution bottle must be procured and stocked for the treatment of preeclampsia and eclampsia. We aim to evaluate technical feasibility and commercial viability of such an $MgSO_4$ dilution bottle to ascertain how we should best proceed with this concept.

Achievements to Date

- Scanned national essential medicines lists of countries in sub-Saharan Africa to understand how $MgSO_4$ is listed.
- Determined that either glass or plastic (high-density polyethylene) is appropriate for the dilution bottle based on a literature review. Also, based on lab testing as well as a literature review, identified that a minimum of 75 mL is required in order to have sufficient headspace in a sealed bottle to allow for the smooth withdrawal of $MgSO_4$.
- Engaged with one of the largest manufacturers of $MgSO_4$ to understand what the pros and cons are of manufacturing such a dilution bottle. This discussion led to an alternative concept for the $MgSO_4$ dilution bottle (i.e., a dilution bottle that contains water for injection [WFI], instead of $MgSO_4$, with a pre-marked fill line so that 50% $MgSO_4$ can be added to make a 20% $MgSO_4$ solution).
- Preparation for a concept evaluation with policymakers, procurement officials, and service providers in two countries is well under way. We will leverage the existing activity for the ready-to-use pack under the UN Commission for Life-Saving Commodities for this concept evaluation. The concept of both the $MgSO_4$ and WFI dilution bottles will be evaluated as components of this ready-to-use pack using prototypes created by the 3D printer at PATH.
- The concept of both the $MgSO_4$ and WFI dilution bottles was evaluated in Ethiopia and Uganda in January 2015. The results of this concept evaluation were analyzed, and the report was disseminated in May 2015.

Upright Resuscitator Video Analysis

This study was undertaken to determine if ventilation technique used during simulated neonatal resuscitation with the conventional and upright resuscitator could be correlated with lung function results, such as the tidal volume and peak inspiratory pressure. These criteria, if identified, may be useful in training programs. The objectives of this effort are to: (1) review the key components in the method of providing bag and mask ventilation that are likely to influence ventilation and correlate these with key lung function parameters, such as tidal volume and peak inspiratory pressure; and (2) identify components, if any, that may be useful in training programs to promote adequate ventilation without producing excessive tidal volumes and peak inspiratory pressures. A draft manuscript has been prepared (see abstract below) and we anticipate submitting it by the end of December 2015. We expect the article to be published in 2016.

Structured Abstract

Title: Ventilation Techniques Used with Two Designs of Neonatal Resuscitators.

Background: A new self-inflating resuscitation bag has been developed for low-resource countries, with a vertically oriented bag and a larger-volume (320 ml) and improved mask design.

Objective: Assess impact of techniques of simulated ventilation and resuscitator design on tidal volume (TV) and peak inspiratory pressure (PIP).

Methods: TV and PIP were measured on a test lung with low compliance followed by normal compliance, as 38 participants ventilated a manikin using the two resuscitators (horizontal resuscitator [HR] and upright resuscitator [UR]), in random order. Observers who were blinded to TV/PIP values independently reviewed 32 videos of ventilation; the observers could document mask hold, number of fingers squeezing the bag, and degree of bag squeeze. These were correlated to TV and PIP.

Results: The most common types of mask holds were the "OK" (as in the OK hand gesture) rim hold and two-point hold. There was no significant difference in TV generated by the UR compared with the HR with low compliance, except with the use of OK hold. With normal compliance, high TV was generated with both resuscitators, but TV was significantly higher with the UR with the OK hold, when more than two fingers squeezed the bag and when more than half the bag was squeezed.

Conclusions: High TV was observed with both resuscitators with normal compliance, but more so with the UR with the OK hold and with excessive squeezing of the bag. This may be due to the larger capacity of the bag or due to a better mask seal with the UR. The upright orientation and improved mask design in the UR likely helped support better mask seal, but they resulted in higher tidal volumes. Excessive squeezing of the bag promoted needless high tidal volumes especially during normal compliance, which also suggests the lack of recognition of changes in compliance. Capacity-building needs to address the importance of mask seal and avoidance of excessive squeezing of the bag and improved recognition of changes in compliance.

Performance and Monitoring

Performance and Monitoring

A majority of HealthTech performance and monitoring data are reported yearly in aggregate across all projects, some data will be compiled at the project's end. Table 1 below shows the data collected as of Year 4. Table 2, on page 44 describes the indicators in detail.

Table 1. HealthTech Performance and Monitoring Data

Indicator	Y1 Data	Y2 Data	Y3 Data	Y4 Data	Y5 Data
Number of high potential technologies identified	4	15	6	11	
Number of technologies or components evaluated in a lab/bench or controlled setting	6	8	4	5	
Number of technologies being designed with user input	4	3	2	11	
Number of technologies in the introduction phase	0	3	1	2	
Number of technologies evaluated in the field implementation phase	1	1	0	3	
Number of suppliers/manufacturers with assessed capacity to enter the market with a technology that appropriately meets product specifications	5	13	8	18	
Number of technologies with potential for sustainable supply	4	6	3	5	
Unit cost/price of each technology compared to existing technologies *(reported at project end)*	-	-	-	-	
Number of successful technology transfers *(reported at project end)*	-	-	-	-	
Number of research/development partnerships formalized	6	14	8	16	
Level of use of HealthTech V information about product category or technology by external groups	Downloads/views from the PATH website: 7,691 Conferences where information was disseminated: 10	Downloads/views from the PATH website: 18,884 Conferences where information was disseminated: 26	Downloads/views from the PATH website: 29,766 Conferences where information was disseminated: 12	Downloads/views from the PATH website: 37,748 Conferences where information was disseminated: 27	

Indicator	Y1 Data	Y2 Data	Y3 Data	Y4 Data	Y5 Data
Number of products that are registered for use in developed or developing countries	1	4	2	3	
Use rates of new technologies *(reported at project end)*	-	-	-	-	
Amount of outside funds used to support HealthTech V	$522,925	$2,733,098	$671,250	$1,744,391	
Coverage of new technologies at facility/district level *(reported at project end)*	-	-	-	-	
Availability of supply of new product *(reported at project end)*	-	-	-	-	
Number of guidelines/policies and decisions approved that support broader scale-up of product use at a global, national, or subnational level *(reported at project end)*	-	-	-	-	

Table 2. HealthTech Performance and Monitoring Matrix

Indicator	Indicator Definition	Indicator Measurement	Source of Data	Method of Data Collection	Schedule of Data Collection	Type of Indicator
Intermediate Result 1: Increased availability of innovative and affordable health technologies						
IR 1.1: Identification and prioritization of new and promising technologies to address health development challenges						
Number of high potential technologies identified	Program's contribution to identification of high potential technologies through landscape analyses that explore acceptability, potential markets, technical feasibility, barriers, intellectual property (IP) issues, costs, financial factors, and stakeholder views.	Number of target product profiles (TPP) for high potential technologies completed	Project records	Landscape reviews and stakeholder feedback	As needed	Output
IR 1.2: Development of viable health technologies that are appropriate, affordable, and acceptable for distribution and use in low-resource settings and show promise for sustainable market development						
Number of technologies or components evaluated in a lab/bench or controlled setting	Number of products reaching validation phase. Tracks outcomes and recommendations to discontinue, improve existing design, or move to field evaluation.	Number of products disaggregated by stage completed	Evaluation report	Lab/bench-based protocols and studies	As needed per technology	Output
Number of technologies being designed with user input	Number of user assessments per technology. Tracks outcomes and recommendations to discontinue, improve existing design, or move to field evaluation.	Number of products disaggregated by stage completed	Evaluation report	User assessment studies, expert consultations	As needed, per technology	Output
Number of technologies in the introduction phase	Number of technologies that progress to introduction phase.	Number of technologies evaluated through pilot testing	Record review—evaluation reports	Special studies: using mixed methods	Annually	Output
Number of technologies evaluated in the field implementation phase	Number of technologies that progress to field implementation phase.	Number of technologies introduced at regional, subnational, or national level	Project records	Special studies: using mixed methods	TBD by technology	Output
Number of suppliers/manufacturers with assessed capacity to enter the market with a technology that appropriately meets product specifications	Number of suppliers who have the necessary capacity to supply a product meeting established product requirements.	Number of identified suppliers/ manufacturers with substantial supply capability of the technology	Project records	Supplier assessments	TBD by technology	Output
Number of technologies with potential for sustainable supply	Number of technologies that have been analyzed in terms of value proposition/business case/building toward sustainable supply.	Number of technologies with market requirements established	Project records	Project reports	TBD by technology	Output
Unit cost/price of each technology compared to existing technologies	Unit cost/price of new technology compared to existing technologies at comparable stage of production.	Dollars per unit at prototype stages; initial manufacturing; and/or projected cost at various levels of scale-up	Project records	Project reports	Project end	Output
Number of successful technology transfers	Number of entities receiving knowledge, expertise, or technology capacity to enable them to produce product according to established specifications. Will solicit feedback on quality of transfer and actions beyond the initial transfer of knowledge/resources.	Evidence of product manufactured to product specifications; increase in knowledge levels; increase in technical capacity	Project and manufacturing records—technology transfer partner survey	Project reports; follow-up survey to possibly include interviews	Project end	Output
IR 1.2a: Innovation fostered to identify new concepts and opportunities for technology development						
Number of research/development partnerships formalized	Total number/type of partnerships between US, international, private, and research or manufacturing institutions.	Number of partnerships formed	Project records	Routine data collection through project reporting	Annually	Process
Level of use of HealthTech V information about product category or technology by external groups	Total number of instances that information about technology opportunities is accessed by external groups.	Number of technology update reports downloaded from PATH website; number of times technology information disseminated at conferences/meetings	Project records	Records review	Annually	Outcome

Indicator	Indicator Definition	Indicator Measurement	Source of Data	Method of Data Collection	Schedule of Data Collection	Type of Indicator
Intermediate Result 2: Increased use of new health technologies in developing countries						
IR 2.1: Introduction of innovative health technologies in developing country settings, bridging the "research to use" gap						
Number of products that are registered for use in developed or developing countries	Evidence of regulatory approval in developed/developing countries including international quality assurance schemes such as World Health Organization prequalification and/or product registration.	Number of regulatory approvals per product	Approval from authorizing agencies	Routine data collection through project reporting	Annually	Output
Use rates of new technologies	Rates will be calculated differently for each given technology, (i.e., estimations of sales/procurement; facility, private sector, or household data).	Number of users disaggregated per technology	Project and partner records	Special studies	Project end	Outcome
Amount of outside funds used to support HealthTech V	Funds leveraged through commercial partnerships. Identifies new partners, catalyzed by commitment, competition from the private sector. Total co-investments disaggregated by private, public, and nonprofit partners and by project.	Dollars allocated	Project and partner records	Total amounts disaggregated by partner, sector, and project	Annually	Outcome
IR 2.2: Scale-up to global access and use of health technologies						
Coverage of new technologies at facility/district level	Rates of coverage for technologies in use. Depending on the technology, coverage rates would be measured differently.	Portion of the population with access to the technology	Population records	Special studies	Project end	Outcome
Availability of supply of new product	Number of units that manufacturers are producing.	Number of product units produced (absolute and as percentage of total market estimate (if possible) TBD by product type	Partner records	Record review	Project end	Outcome
Number of guidelines/policies and decisions approved that support broader scale-up of product use at a global, national, or subnational level	Support from global and national policy/decision-making bodies to create enabling environment for technology introduction.	Number of guidelines or policies created that support scale-up of specific technologies	Policy review and partner records	Routine data collection through project reporting	Project end	Outcome